



Human Obesity and Related Health Issues

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ABSTRACT: Obesity increases the risk of several debilitating, and deadly diseases, including **diabetes, heart disease, and some cancers**. It does this through a variety of pathways, some as straightforward as the mechanical stress of carrying extra pounds and some involving complex changes in hormones and metabolism. People who have overweight or obesity*, compared to those with healthy weight, are at increased risk for many serious diseases and health conditions. These include:

All-causes of death (mortality), High blood pressure (hypertension), High LDL cholesterol, low HDL cholesterol, or high levels of triglycerides (dyslipidemia), Type 2 diabetes, Coronary heart disease, Stroke, Gallbladder disease, Osteoarthritis (a breakdown of cartilage and bone within a joint), Sleep apnea and breathing problems, Many types of cancer, Low quality of life, Mental illness such as clinical depression, anxiety, and other mental disorders, Body pain and difficulty with physical functioning

KEYWORDS: obesity, heart, death, hypertension, cancer, anxiety, disorders, pain, osteoarthritis

I. INTRODUCTION

Obesity is a complex disease involving an excessive amount of body fat. Obesity isn't just a cosmetic concern. It's a medical problem that increases the risk of other diseases and health problems, such as heart disease, diabetes, high blood pressure and certain cancers.

There are many reasons why some people have difficulty losing weight. Usually, obesity results from inherited, physiological and environmental factors, combined with diet, physical activity and exercise choices.

The good news is that even modest weight loss can improve or prevent the health problems associated with obesity. A healthier diet, increased physical activity and behavior changes can help you lose weight. Prescription medications and weight-loss procedures are additional options for treating obesity.[1,2]

Body mass index (BMI) is often used to diagnose obesity. To calculate BMI, multiply weight in pounds by 703, divide by height in inches and then divide again by height in inches. Or divide weight in kilograms by height in meters squared.



BMI	Weight status
Below 18.5	Underweight
18.5-24.9	Normal
25.0-29.9	Overweight
30.0 and higher	Obesity

Asians with BMI of 23 or higher may have an increased risk of health problems.

For most people, BMI provides a reasonable estimate of body fat. However, BMI doesn't directly measure body fat, so some people, such as muscular athletes, may have a BMI in the obesity category even though they don't have excess body fat.[3,4]

Many doctors also measure a person's waist circumference to help guide treatment decisions. Weight-related health problems are more common in men with a waist circumference over 40 inches (102 centimeters) and in women with a waist measurement over 35 inches (89 centimeters).

II. SOME HEALTH RISKS OF OVERWEIGHT AND OBESITY

Type 2 diabetes

Type 2 diabetes is a disease that occurs when your blood glucose, also called blood sugar, is too high. About 8 out of 10 people with type 2 diabetes are overweight or have obesity.⁸ Over time, high blood glucose leads to problems such as heart disease, stroke, kidney disease, eye problems, nerve damage, and other health problems.

If you are at risk for type 2 diabetes, losing 5 to 7 percent of your body weight and getting regular physical activity may prevent or delay the onset of type 2 diabetes.[5,6]

High blood pressure

High blood pressure, also called hypertension, is a condition in which blood flows through your blood vessels with a force greater than normal. High blood pressure can strain your heart, damage blood vessels, and raise your risk of heart attack, stroke, kidney disease, and death.

Heart disease

Heart disease is a term used to describe several problems that may affect your heart. If you have heart disease, you may have a heart attack, heart failure, sudden cardiac death, angina NIH external link, or an abnormal heart rhythm. High



blood pressure, abnormal levels of blood fats, and high blood glucose levels may raise your risk for heart disease. Blood fats, also called blood lipids, include HDL cholesterol, LDL cholesterol, and triglycerides.

Losing 5 to 10 percent of your weight may lower your risk factors for developing heart disease. If you weigh 200 pounds, this means losing as little as 10 pounds. Weight loss may improve blood pressure, cholesterol levels, and blood flow.[7,8]

Stroke

Stroke is a condition in which the blood supply to your brain is suddenly cut off, caused by a blockage or the bursting of a blood vessel in your brain or neck. A stroke can damage brain tissue and make you unable to speak or move parts of your body. High blood pressure is the leading cause of strokes.

Sleep apnea

Sleep apnea is a common disorder in which you do not breathe regularly while sleeping. You may stop breathing altogether for short periods of time. Untreated sleep apnea may raise your risk of other health problems, such as type 2 diabetes and heart disease.

Metabolic syndrome

Metabolic syndrome is a group of conditions that put you at risk for heart disease, diabetes, and stroke. These conditions are[9,10]

- high blood pressure
- high blood glucose levels
- high triglyceride levels in your blood
- low levels of HDL cholesterol (the “good” cholesterol) in your blood
- too much fat around your waist

Fatty liver diseases

Fatty liver diseases are conditions in which fat builds up in your liver. Fatty liver diseases include nonalcoholic fatty liver disease (NAFLD) and nonalcoholic steatohepatitis (NASH). Fatty liver diseases may lead to severe liver damage, cirrhosis, or even liver failure.

Osteoarthritis

Osteoarthritis is a common, long-lasting health problem that causes pain, swelling, and reduced motion in your joints. Being overweight or having obesity may raise your risk of getting osteoarthritis by putting extra pressure on your joints and cartilage.

Gallbladder diseases

Overweight and obesity may raise your risk of getting gallbladder diseases, such as gallstones and cholecystitis. Imbalances in substances that make up bile cause gallstones. Gallstones may form if bile contains too much cholesterol.[11,12]



Some cancers

Cancer NIH external link is a collection of related diseases. In all types of cancer, some of the body's cells begin to divide without stopping and spread into surrounding tissues. Overweight and obesity may raise your risk of developing certain types of cancer NIH external link.

Kidney disease

Kidney disease means that your kidneys are damaged and can't filter blood like they should. Obesity raises the risk of diabetes and high blood pressure, the most common causes of kidney disease. Even if you don't have diabetes or high blood pressure, obesity itself may promote kidney disease and quicken its progress.

Pregnancy problems

Overweight and obesity raise the risk of health problems that may occur during pregnancy. Pregnant women who are overweight or obese may have a greater chance of [13,14]

- developing gestational diabetes
- having preeclampsia—high blood pressure during pregnancy, which can cause severe health problems for mother and baby if left untreated
- needing a cesarean section NIH external link, or C-section and, as a result, taking longer to recover after

Emotional and social problems are linked to overweight and obesity

Overweight and obesity are associated with mental health problems such as depression NIH external link. People who deal with overweight and obesity may also be the subject of weight bias and stigma from others, including health care providers. This can lead to feelings of rejection, shame, or guilt—further worsening mental health problems.

III. DISCUSSION

Overweight and obesity are defined as abnormal or excessive fat accumulation that presents a risk to health. A body mass index (BMI) over 25 is considered overweight, and over 30 is obese. The issue has grown to epidemic proportions, with over 4 million people dying each year as a result of being overweight or obese in 2017 according to the global burden of disease.

Rates of overweight and obesity continue to grow in adults and children. From 1975 to 2016, the prevalence of overweight or obese children and adolescents aged 5–19 years increased more than four-fold from 4% to 18% globally.

Obesity is one side of the double burden of malnutrition, and today more people are obese than underweight in every region except sub-Saharan Africa and Asia. Once considered a problem only in high-income countries, overweight and obesity are now dramatically on the rise in low- and middle-income countries, particularly in urban settings. The vast majority of overweight or obese children live in developing countries, where the rate of increase has been more than 30% higher than that of developed countries [15,16]

Newer research has focused on methods of identifying healthier obese people by clinicians, and not treating obese people as a monolithic group. Obese people who do not experience medical complications from their obesity are sometimes called (metabolically) healthy obese, but the extent to which this group exists (especially among older people) is in dispute. The number of people considered metabolically healthy depends on the definition used, and there is no universally accepted definition. There are numerous obese people who have relatively few metabolic abnormalities, and a minority of obese people have no medical complications. The guidelines of the American



Association of Clinical Endocrinologists call for physicians to use risk stratification with obese patients when considering how to assess their risk of developing type 2 diabetes.

IV. RESULTS

In 2014, the BioSHaRE–EU Healthy Obese Project (sponsored by Maelstrom Research, a team under the Research Institute of the McGill University Health Centre) came up with two definitions for healthy obesity, one more strict and one less so.[17,18]

BioSHaRE Healthy Obese (HOP) Project Criteria (2014)

A patient must have a body mass index ≥ 30 , and all of the following:

	Less strict	More strict
Blood pressure measured as follows, with no pharmaceutical help		
Overall (mmHg)	≤ 140	≤ 130
Systolic (mmHg)	N/A	≤ 85
Diastolic (mmHg)	≤ 90	N/A
Blood sugar level measured as follows, with no pharmaceutical help		
Blood glucose (mmol/l)	≤ 7.0	≤ 6.1
Triglycerides measured as follows, with no pharmaceutical help		
Fasting (mmol/l)	≤ 1.7	
Non-fasting (mmol/l)	≤ 2.1	
High-density lipoprotein measured as follows, with no pharmaceutical help		
Men (mmol/l)	> 1.03	
Women (mmol/l)	> 1.3	
No diagnosis of any cardiovascular disease		

To come up with these criteria, BioSHaRE controlled for age and tobacco use, researching how both may effect the metabolic syndrome associated with obesity, but not found to exist in the metabolically healthy obese

Management of obesity can include lifestyle changes, medications, or surgery. Although many studies have sought effective interventions, there is currently no evidence-based, well defined, and efficient intervention to prevent obesity.[19,20]



The main treatment for obesity consists of weight loss via healthy nutrition and increasing physical exercise.[2][3][4][5] A 2007 review concluded that certain subgroups such as those with type 2 diabetes and women who undergo weight loss show long-term benefits in all-cause mortality, while long-term outcomes for men are "not clear and need further investigation."

The most effective treatment for obesity is bariatric surgery. Surgery for severe obesity is associated with long-term weight loss and decreased overall mortality. One study found a weight loss of between 14% and 25% (depending on the type of procedure performed) at 10 years, and a 29% reduction in all cause mortality when compared to standard weight loss measures.[8] Another study also found reduced mortality in those who underwent bariatric surgery for severe obesity.

In June 2021, the US Food and Drug Administration (FDA) approved semaglutide injection sold under the brand name Wegovy for long-term weight management in adults. It is associated with a loss of 6-12% of body weight along with mild gastrointestinal side effects.

Another medication, orlistat, is widely available and approved for long-term use. Its use produces modest weight loss, with an average of 2.9 kg (6.4 lb) at 1 to 4 years, but there is little information on how these medications affect longer-term complications of obesity. Its use is associated with high rates of gastrointestinal side effects. Diet programs can produce short-term weight loss and, to a lesser extent, over the long-term. Greater weight loss results, including amongst underserved populations, are achieved when proper nutrition is regularly combined with physical exercise and counseling. Dietary and lifestyle changes are effective in limiting excessive weight gain in pregnancy and improve outcomes for both the mother and the child.[21,22]

Diets to promote weight loss can be divided into four categories: low-fat, low-carbohydrate, low-calorie, and very low calorie. Many dietary patterns are effective. A meta-analysis of six randomized controlled trials found no difference between three of the main diet types (low calorie, low carbohydrate, and low fat), with a 2–4 kilograms (4.4–8.8 lb) weight loss in all studies. At two years these three methods resulted in similar weight loss irrespective of the macronutrients emphasized. High protein diets do not appear to make any difference. A diet high in added sugars such as those in soft drinks increases weight. There is evidence that dieting alone can be effective for weight loss and improving health for obese individuals. Dieting for calorie restriction is advised for overweight individuals by the Dietary Guidelines for Americans and United Kingdom's NICE.

With use, muscles consume energy derived from both fat and glycogen. Due to the large size of leg muscles, walking, running, and cycling are the most effective means of exercise to reduce body fat. Exercise affects macronutrient balance. During moderate exercise, equivalent to a brisk walk, there is a shift to greater use of fat as a fuel. To maintain health, the American Heart Association recommends a minimum of 30 minutes of moderate exercise at least 5 days a week.

The Cochrane Collaboration found that exercising alone led to limited weight loss. In combination with diet, however, it resulted in a 1 kilogram weight loss over dieting alone. A 1.5 kilograms (3.3 pounds) loss was observed with a greater degree of exercise. Even though exercise as carried out in the general population has only modest effects, a dose response curve is found, and very intense exercise can lead to substantial weight loss. During 20 weeks of basic military training with no dietary restriction, obese military recruits lost 12.5 kg (28 lb). High levels of physical activity seem to be necessary to maintain weight loss. A pedometer appears useful for motivation. Over an average of 18-weeks of use physical activity increased by 27% resulting in a 0.38 decreased in BMI.[23,24]

Signs that encourage the use of stairs as well as community campaigns have been shown to be effective in increasing exercise in a population. The city of Bogota, Colombia for example blocks off 113 kilometers (70 mi) of roads every Sunday and on holidays to make it easier for its citizens to get exercise. These pedestrian zones are part of an effort to combat chronic diseases, including obesity. In an effort to combat the issue, a primary school in Australia instituted a standing classroom in 2013. There is evidence that exercise alone is not sufficient to produce meaningful weight loss, but combining dieting and exercise provide the greatest health benefits and weight loss on the long term.

Weight loss programs involve lifestyle changes including diet modifications, physical activity and behavior therapy. This may involve eating smaller meals, cutting down on certain types of food, and making a conscious effort to exercise more. These programs also enable people to connect with a group of others who are attempting to lose weight, in the hopes that participants will form mutually motivating and encouraging relationships. Since 2013, the United States guidelines recommend to treat obesity as a disease and actively treat obese people for weight loss. A number of popular programs exist, including Weight Watchers, Overeaters Anonymous, and Jenny Craig. These appear to provide modest weight loss (2.9 kg; 6.4 lb) over dieting on one's own (0.2 kg; 0.44 lb) over a two-year period, similarly to non-commercial diets. Internet-based programs appear to be ineffective. The Chinese government has introduced a number of "fat farms" where obese children go for reinforced exercise, and has passed a law which requires students to exercise or play sports for an hour a day at school.

In a structured setting with a trained therapist, these interventions produce an average weight loss of up to 8 kg in 6 months to 1 year, and 67% of people who lost greater than 10% of their body mass maintained or continued to lose weight one year later. There is a gradual weight regain after the first year of about 1 to 2 kg per year, but on the long-term this still results in a weight loss.[25,26]

Attending group meetings for weight reduction programmes rather than receiving one-on-one support may increase the likelihood that obese people will lose weight. Those who participated in groups had more treatment time and were more likely to lose enough weight to improve their health. Study authors suggested that one explanation for the difference is that group participants spent more time with the clinician (or whoever delivered the programme) than those receiving one-on-one support.

Comprehensive diet programs, providing counseling, targets for calorie intake and exercise, may be more efficient than dieting without guidance ("self-help"), although the evidence is very limited. Following comprehensive lifestyle modifications, the average maintained weight loss is more than 3 kg (6.6 lb) or 3% of total body mass, and could be sustained for five years, and up to 20% of the individuals maintain a weight loss of at least 10% (average of 33 kg). There is some evidence that fast weight loss produce greater long-term weight loss than gradual weight loss. Moderate on-site comprehensive lifestyle changes produce a greater weight loss than usual care, of 2 to 4 kg on average in 6 to 12 months. High-intensity comprehensive programs usually yield more weight loss than moderate or low-intensity, with about 35% to 60% of overweight individuals maintaining more than 5 kg weight loss after 2 years. The NICE devised a set of essential criteria to be met by commercial weight management organizations to be approved. The Transtheoretical Model (TTM) has been used as a framework to assist the design of lifestyle modification programmes, including weight management. A systematic review found that there is insufficient evidence to draw conclusions regarding the effects of TTM-based programs targeting weight loss that included dietary or physical activity interventions, or both (and also combined with other interventions), on sustainable weight loss (one year or longer) in overweight and obese adults. However, very low quality evidence points that this approach may induce positive changes in physical activity and dietary habits, such as increased in exercise duration and frequency, improvement in fruits and vegetables consumption, and reduced dietary fat intake.[27]

V. CONCLUSIONS

Several anti-obesity medications are currently approved by the FDA for long term use.

- Semaglutide (Wegovy) is currently approved by the FDA for long-term use, being associated with a 6-12% loss in body weight compared to placebo.
- The combination drug phentermine/topiramate (Qsymia) is approved by the FDA as an addition to a reduced-calorie diet and exercise for chronic weight management.
- Orlistat reduces intestinal fat absorption by inhibiting pancreatic lipase. Over the longer term, average weight loss on orlistat is 2.9 kg (6.4 lb). It leads to a reduced incidence of diabetes, and has some effect on cholesterol. However, there is little information on how it affects the longer-term complications or outcomes of obesity.
- Racemic amphetamine, phendimetrazine, diethylpropion, and phentermine are approved by the FDA for short term use
 - Bupropion, topiramate, and zonisamide are sometimes used off-label for weight loss.



- The usefulness of certain drugs depends upon the comorbidities present. Metformin is preferred in overweight diabetics, as it may lead to mild weight loss in comparison to sulfonylureas or insulin. The thiazolidinediones, on the other hand, may cause weight gain, but decrease central obesity. Diabetics also achieve modest weight loss with fluoxetine and orlistat over 12–57 weeks.
- Rimonabant (Acomplia), another drug, had been withdrawn from the market. It worked via a specific blockade of the endocannabinoid system. It has been developed from the knowledge that cannabis smokers often experience hunger, which is often referred to as "the munchies". It had been approved in Europe for the treatment of obesity but has not received approval in the United States or Canada due to safety concerns. European Medicines Agency in October 2008 recommended the suspension of the sale of rimonabant as the risk seem to be greater than the benefits.
- Sibutramine (Meridia), which acts in the brain to inhibit deactivation of the neurotransmitters, thereby decreasing appetite was withdrawn from the UK market in January 2010 and United States and Canadian markets in October 2010 due to cardiovascular concerns. In 2010 it was found that sibutramine increases the risk of heart attacks and strokes in people with a history of cardiovascular disease.
- Fenfluramine and dexfenfluramine were withdrawn from the market in 1997, while ephedrine (found in the traditional Chinese herbal medicine má huáng made from the Ephedra sinica) was removed from the market in 2004.
- Lorcaserin used to be approved by the Food and Drug Administration for use in the treatment of obesity before being withdrawn due to cancer risk.
- Recombinant human leptin is very effective in those with obesity due to congenital complete leptin deficiency via decreasing energy intake and possibly increases energy expenditure. This condition is, however, rare and this treatment is not effective for inducing weight loss in the majority of people with obesity. It is being investigated to determine whether or not it helps with weight loss maintenance.
- Though hypothesized that supplementation of vitamin D may be an effective treatment for obesity, studies do not support this. There is also no strong evidence to recommend herbal medicines for weight loss.[28]

Bariatric surgery ("weight loss surgery") is the use of surgical intervention in the treatment of obesity. As every operation may have complications, surgery is only recommended for severely obese people (BMI > 40) who have failed to lose weight following dietary modification and pharmacological treatment. Weight loss surgery relies on various principles: the two most common approaches are reducing the volume of the stomach (e.g. by adjustable gastric banding and vertical banded gastroplasty), which produces an earlier sense of satiation, and reducing the length of bowel that comes into contact with food (e.g. by gastric bypass surgery or endoscopic duodenal-jejunal bypass surgery), which directly reduces absorption. Band surgery is reversible, while bowel shortening operations are not. Some procedures can be performed laparoscopically. Complications from weight loss surgery are frequent.

Surgery for severe obesity is associated with long-term weight loss and decreased overall mortality. One study found a weight loss of between 14% and 25% (depending on the type of procedure performed) at 10 years, and a 29% reduction in all cause mortality when compared to standard weight loss measures. A marked decrease in the risk of diabetes mellitus, cardiovascular disease and cancer has also been found after bariatric surgery. Marked weight loss occurs during the first few months after surgery, and the loss is sustained in the long term. In one study there was an unexplained increase in deaths from accidents and suicide, but this did not outweigh the benefit in terms of disease prevention. When the two main techniques are compared, gastric bypass procedures are found to lead to 30% more weight loss than banding procedures one year after surgery. For obese individuals with non-alcoholic fatty liver disease (NAFLD), bariatric surgery improves or cures the liver.

A preoperative diet such as low-calorie diets or very-low-calorie diet, is usually recommended to reduce liver volume by 16-20%, and preoperative weight loss is the only factor associated with postoperative weight loss. Preoperative weight loss can reduce operative time and hospital stay. although there is insufficient evidence whether preoperative weight loss may be beneficial to reduce long-term morbidity or complications. Weight loss and decreases in liver size may be independent from the amount of calorie restriction.

Ileocecal bypass, in which the digestive tract is rerouted to bypass the small intestine, was an experimental surgery designed as a remedy for morbid obesity.



The effects of liposuction on obesity are less well determined. Some small studies show benefits while others show none. A treatment involving the placement of an intragastric balloon via gastroscopy has shown promise. One type of balloon led to a weight loss of 5.7 BMI units over 6 months or 14.7 kg (32 lb). Regaining lost weight is common after removal, however, and 4.2% of people were intolerant of the device.

An implantable nerve simulator which improves the feeling of fullness was approved by the FDA in 2015.

In 2016 the FDA approved an aspiration therapy device that siphons food from the stomach to the outside and decreases caloric intake. As of 2015 one trial shows promising results.

Much of the Western world has created clinical practice guidelines in an attempt to address rising rates of obesity. Australia, Canada, the European Union, and the United States have all published statements since 2004.

In a clinical practice guideline by the American College of Physicians, the following five recommendations are made:

People with a BMI of over 30 should be counseled on diet, exercise and other relevant behavioral interventions, and set a realistic goal for weight loss.

If these goals are not achieved, pharmacotherapy can be offered. The person needs to be informed of the possibility of side-effects and the unavailability of long-term safety and efficacy data.

Drug therapy may consist of sibutramine, orlistat, phentermine, diethylpropion, fluoxetine, and bupropion. Evidence is not sufficient to recommend sertraline, topiramate, or zonisamide.

In people with a BMI over 40 who fail to achieve their weight loss goals (with or without medication) and who develop obesity-related complications, referral for bariatric surgery may be indicated. The person needs to be aware of the potential complications.

Those requiring bariatric surgery should be referred to high-volume referral centers, as the evidence suggests that surgeons who frequently perform these procedures have fewer complications.

A clinical practice guideline by the US Preventive Services Task Force (USPSTF) concluded that the evidence is insufficient to recommend for or against routine behavioral counseling to promote a healthy diet in unselected people in primary care settings, but that intensive behavioral dietary counseling is recommended in those with hyperlipidemia and other known risk factors for cardiovascular and diet-related chronic disease. Intensive counseling can be delivered by primary care clinicians or by referral to other specialists, such as nutritionists or dietitians.

Canada developed and published evidence-based practice guidelines in 2006. The guidelines attempt to address the prevention and management of obesity at both the individual and population levels in both children and adults. The European Union published clinical practice guidelines in 2008 in an effort to address the rising rates of obesity in Europe. Australia came out with practice guidelines in 2004.[29]

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